Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2014R1A1A1004790).

Contact: Se-yun Cheon, chunsay1008@naver.com

http://dx.doi.org/10.1016/j.imr.2015.04.045

P1.039

Chicoric acid inhibits the production of pro-inflammatory cytokines through inhibition of NF-κB signaling pathway in HMC-1 human mast cells

Na-Young Lee, Kyung-Sook Chung, Hyo-Jin An

Department of Pharmacology, College of Oriental Medicine, Sangji University

Purpose: A great number of people are suffering from allergic inflammatory disease such as asthma, atopic dermatitis, and sinusitis. Therefore discovery of drugs for the treatment of these diseases is an important subject in human health. Chicoric acid is a natural phenolic compound that has been reported to inhibit HIV integrase and to exhibit antioxidant activities. Although these biological effects of chicoric acid have been conducted, no anti-allergic inflammatory effect of chicoric acid has been reported in HMC-1 human mast cells.

Methods: HMC-1 human mast cells were incubated with chicoric acid (μM) and/or phorbol 12-myristate 13-acetate (PMA) plus A23187. Cytokine production and relevant factors expression in activated HMC-1 cells were determined by enzyme- linked immunosorbent assay (ELISA), western blot and quantitative reverse transcription-polymerase chain reaction (qRT-PCR) analysis. Also, the involvement of the mitogen-activated protein kinases (MAPKs) and nuclear factor-κB (NF- κB) in activated HMC-1 cells were studied.

Results: Chicoric acid decreased expression of pro-inflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-1β. The inhibitory effect of chicoric acid on theses pro-inflammatory cytokines was related with c-Jun N- terminal kinases (JNK), and p38 MAPK, NF-κB. We also found that chicoric acid blocked nuclear translocation of NF- κB inhibiting the phosphorylation of IκBα and suppressed NF-κB transcriptional activity in stimulated HMC-1 cells.

Conclusion: Our results showed that chicoric acid down-regulates mast cell-derived allergic inflammatory reactions by blocking histamine release and expression of pro-inflammatory cytokines. In light of in vitro anti-allergic inflammatory effects, chicoric acid could be a beneficial anti-allergic inflammatory agent. This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2014R1A1A2008663).

Contact: Na-Young Lee, lny4674@hanmail.net

http://dx.doi.org/10.1016/j.imr.2015.04.046

P1.040

Water extract of Magnolia officinalis cortex Inhibits Osteoclastogenesis and Bone resorption by Downregulation of Nuclear Factor of Activated T Cells

Ki-Shuk Shim, Taesoo Kim, Hyunil Ha, Chung-Jo Lee, Jin Yeul Ma

Korea Institute of Oriental Medicine

Purpose: Magnolia officinalis cortex has been traditionally used to treat stomach and intestine diseases in Traditional Chinese Medicine. In this study, we investigated the effect of water extract of Magnolia officinalis cortex (WEMC) on osteoclast differentiation and function.

Methods: We examined the effect of water extract of Magnolia officinalis cortex (WEMC) in activator of nuclear factor-κB ligand (RANKL)-induced osteoclast differentiation and resorption activity. Osteoclast differentiation of bone marrow-derived macrophages was determined by tartrate-resistant acid phosphatase activity assay. RANKL-related transcription factors and signaling factors were analyzed by Western blot and real-time PCR. Bone resorption function of mature osteoclasts was evaluated by pit formation assay. The in vivo effect of WEMC on RANKL-induced bone destruction model was investigated by bone loss model.

Results: WEMC inhibited osteoclast differentiation of osteoclast precursor cells induced by RANKL, a key cytokine for osteoclast differentiation. Gallic acid and honokiol were identified in WEMC as active constituents contributing to the inhibitory effect of WEMC on osteoclast differentiation. WEMC suppressed RANKL-induced activation of p38 and NF- NF-kappaB pathways and expression of c-Fos and nuclear factor of activated T cells cytoplasmic 1 (NFATc1), key transcription factors for osteoclast differentiation. Ectopic overexpression of a constitutive active form of NFATc1 rescued the anti-osteoclastogenic effect of WEMC. In addition, WEMC decreased bone resorbing activity of mature osteoclasts. Consistent with the in vitro results, WEMC significantly suppressed RANKL-induced osteoclastic bone resorption and trabecular bone loss in mice.

Conclusion: WEMC might have a therapeutic potential to treat pathological bone diseases by inhibiting osteoclastogenesis and bone resorption.

Contact: Ki-Shuk Shim, angeloshim@kiom.re.kr

http://dx.doi.org/10.1016/j.imr.2015.04.047

P1.041

Phytochemical screening of Pure Chemical compounds by Off-line and On-line Methods Assay

Kwang Jin Lee, Min Jung Gu, Bo Hyoung Lee, Jin Yeul Ma

Korea Institute of Oriental Medicine

Purpose: Generally, OMHs is very effective for anti-cancer, anti-inflammat and anti-virus. It also receives much attention

as drug, functional food and cosmetic material from lots of researchers. In this study, the antioxidant activity of 100 kinds' pure different standard chemical of oriental medicine herbs (OMHs) compounds has been investigated.

Methods: Also, a couple of compounds having noticeable antioxidant activity were screened, identified and quantified by off-line and on-line screening HPLC-ABTS assay.

Results: This work investigates applications of DPPH and ABTS assay for bioactivity screening of 100 different standard chemical, so that the IC50 rates of 17 more practical compounds are determined. The three most practical compounds (Galic acid, Quercetin, Caffeic acid) were screened, identified and quantified, using coupled off-line-ABTS and on-line HPLC-ABTS screening assay.

Conclusion: This result shows that there is a very small different of error between off-line-ABTS method and on-line screening HPLC-ABTS method. The shows that an on-line screening HPLC-ABTS assay can be a powerful technique for the rapid characterization of bioactivity compounds in plant extracts. Moreover, this result can be considered to be applicable to determinations of the basic antioxidant of OMHs and the data base of phytochemical. And use of information of the experiment should facilitate resistance to internal body stress by ROS.

Contact: Kwang Jin Lee, leekj@kiom.re.kr

http://dx.doi.org/10.1016/j.imr.2015.04.048

P1.042

Guibitang, a traditional herbal medicine, induces apoptotic death in A431 cells by regulating the activities of mitogen-activated protein kinases

Nam-Hui Yim, Aeyung Kim, Won-Kyung Cho, Jin Yeul Ma

Korea Institute of Oriental Medicine

Purpose: Guibi-tang (GBT), a traditional herbal formula, mainly has been shown to possess immune regulation, antioxidant and protective effect of the gastric mucosa. In the present study, we explored the mechanism of chemopreventive/chemotherapeutic efficacy of GBT against human squamous cell carcinoma and proved the efficacy of GBT through performing in vivo xenograft assay.

Methods: For analysis of the constituents of GBT, high performance liquid chromatography (HPLC)-DAD system was performed. To detect the anticancer effect of GBT, cell viability assay, caspase activity assay, cell cycle analysis, DNA fragmentation analysis, and Western blot analysis were performed in A431 cells. Furthermore, the inhibitory effect of tumor growth by GBT was evaluated in athymic nude mice inoculated with A431 cells.

Results: GBT showed cytotoxicity against three different squamous cell carcinoma, especially on A431 cells. GBT induced the apoptosis through activating caspase-8 in A431 cells. Inhibition of A431 cell growth by GBT was caused by G1-phase arrest through regulating proteins associated with cell cycle progression including cyclin D1, p21, and p27. Furthermore, GBT regulated the activation of mitogen-activated protein kinases (MAPKs) including extracellular signal- regulated kinase (ERK), p38 and c-Jun NH2-terminal kinase (JNK), and activated p53, a tumor suppressor protein. The inhibitors of MAPKs respectively blocked GBT-induced cell viability, indicating that MAPKs signals play critical role in cell death caused by GBT. In vivo xenografts, daily oral administration of 600 mg/kg GBT efficiently suppressed the tumorigenic growth of A431 cells without side effects.

Conclusion: We first elucidate that GBT stimulates the apoptotic signaling pathway and suppresses the proliferation of A431 cells via regulating MAPKs signaling pathway. Furthermore, GBT significantly inhibits tumor growth of A431 cells without causing systemic toxicity. Based on our study, GBT could be useful in the management of skin cancer as chemoprevention and chemotherapy remedy.

Contact: Nam-Hui Yim, nhyim23@kiom.re.kr

http://dx.doi.org/10.1016/j.imr.2015.04.049

P1.043

Effect of Simiao Yong'an Decoction on Joint Arthritis of Type II Collagen-induced Arthritis in Rats

Ya-nan Wang, Hui Liu, Ji-sheng Zhang, Wei-guo Ma, Yan Lu, Ya-nan Wang, Feng-xian Meng

Dongfang Hospital, The Second Clinical Medical College of Beijing University of Chinese Medicine

Purpose: To address the dffciacy of Simiao Yong'an decoction on the therapy of collagen-induced arthritis (CIA) in rats and identify the mechanism.

Methods: 36 SD rats were randomly divided into 6 groups including control group, model group, positive group, and high-, medium-, low- dose groups of Chinese medicine Simiao Yong'an decoction. The molding method was injecting 0.2 mg collagen on the root of tail each one. Control group and model group were daily gavaged with distilled water (10 ml/kg / d), positive control group was daily gavaged with leflunomide by 1.9 mg/kg. High-, medium-, low-dose group of Chinese medicine was daily gavaged with Simiao Yong'an decoction by 4.2 g/(kg·d), 2.1 g/(kg·d), 1.05 g/(kg·d), ig 12 weeks. The arthritis index(AI) were observed at 0,2,4,6,8,10 and 12 weeks after treatment. The joint pathological changes were observed at the end of treatment. Levels of IL-6,IL-17and TNF-α in serum were examined by ELISA, mRNA transcription levels of IL-6,IL-17and TNF-α in synovial were detected by RT-PCR.

Results: The AI of rats in positive group, and high-, medium-, low- dose groups of Chinese medicine Simiao Yong'an decoction had significantly improvement compared with that in model group($P<0.05$, $P<0.01$). The ankle joint cartilage pathological had an improvement in in positive group, and high-, medium- Chinese medicine groups as compared with model group. mRNA expression of IL-6 and TNF-α were down-regulated in all treatment groups significantly ($P<0.01$) compared with the model group. mRNA expression of IL-17 were down-regulated significantly in positive group, and high-, medium-dose groups of Chinese medicine($P<0.01$).